

REVIEW TOPIC OF THE WEEK

# Obesity, Exercise, Obstructive Sleep Apnea, and Modifiable Atherosclerotic Cardiovascular Disease Risk Factors in Atrial Fibrillation



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## ABSTRACT

Classically, the 3 pillars of atrial fibrillation (AF) management have included anticoagulation for prevention of thromboembolism, rhythm control, and rate control. In both prevention and management of AF, a growing body of evidence supports an increased role for comprehensive cardiac risk factor modification (RFM), herein defined as management of traditional modifiable cardiac risk factors, weight loss, and exercise. In this narrative review, we summarize the evidence demonstrating the importance of each facet of RFM in AF prevention and therapy. Additionally, we review emerging data on the importance of weight loss and cardiovascular exercise in prevention and management of AF. (J Am Coll Cardiol 2015;66:2899-906) © 2015 by the American College of Cardiology Foundation. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Atrial fibrillation (AF) is the most common sustained arrhythmia and represents a rapidly growing epidemic (1). It is projected that the prevalence will rise from 5.2 million in 2010 to 12.1 million in 2030, driven primarily by our aging population (2). AF is associated with increased morbidity, mortality, and rising health care-associated expenses (3,4).

Unsurprisingly, many modifiable risk factors associated with atherosclerotic cardiovascular disease (ASCVD) have also been associated with AF (Central Illustration). Although the most recent AF practice guidelines acknowledge these risk factors, they provide no evidence-based recommendations on diet, exercise, and lifestyle changes in AF primary and secondary prevention (5). In 2013, the Heart Rhythm Society recognized “advancing AF

prevention efforts by focusing on risk modification” as a key research focus (6). Of note, there are numerous other risk factors for AF, such as valvular heart disease, thyroid disease, or chronic obstructive pulmonary disease, which are not thought of as classical risk factors for atherosclerotic heart disease. Such conditions also have known causal relationships with AF and also have implications for management strategies. These other AF risk factors warrant investigation in the work-up of new diagnoses of AF.

## OBESITY AND WEIGHT LOSS

The rise in prevalence of obesity has been well documented, particularly in the United States, where an estimated one-third of adults are obese (7). During

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**ABBREVIATIONS  
AND ACRONYMS**

- AF** = atrial fibrillation
- ASCVD** = atherosclerotic cardiovascular disease
- BMI** = body mass index
- HTN** = hypertension
- MET** = metabolic equivalent
- OSA** = obstructive sleep apnea
- PVI** = pulmonary vein isolation
- RFM** = risk factor modification

the past 5 years, a number of studies have established that obesity is closely linked to AF risk. Body mass index (BMI) is part of prediction models for new-onset AF (8). The connection between obesity and AF has been shown to occur independently of the many comorbidities associated with obesity (9,10). In the ARIC (Atherosclerosis Risk In Communities) study (N = 14,598), 17% of AF risk was attributed to obesity or overweight status (11). In the WHS (Women’s Health Study) (N = 34,309), for every 1 kg/m<sup>2</sup> increase in BMI, the relative AF risk increased by 5% (10). In the Women’s Health Initiative cohort of 93,676 females, for every 1 kg/m<sup>2</sup> increase in BMI, AF relative risk increased by 12%. (12). Interestingly, higher levels of physical activity attenuated the AF risk conferred by obesity (13). BMI >35 kg/m<sup>2</sup> was also associated with increased AF risk by a hazard ratio of 3.50 in young, healthy women (14).

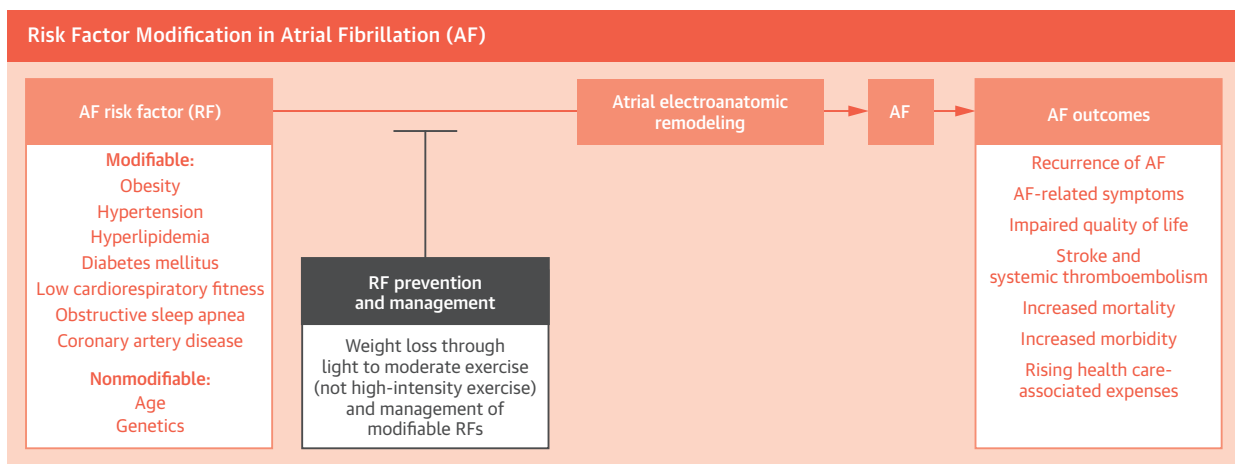
In a recent meta-analysis of 51 studies and 626,603 patients, for every 5 kg/m<sup>2</sup> increase in BMI, there was a 10% to 29% higher relative risk for new-onset or post-operative AF (15). In a subanalysis of 16 studies and 5,864 patients undergoing AF ablation, the risk of AF recurrence increased by 13% for every 5 kg/m<sup>2</sup> increase in BMI (15). Adiposity measures other than BMI have also been associated with increased AF risk. In a Danish registry of 55,273 participants and

13.5 years of follow-up, increased total body fat mass assessed by bioelectrical impedance was associated with higher incidence of AF (16).

Several mechanisms underlie the association between obesity and AF. In a sheep model fed a high-caloric diet, obesity was associated with left atrial enlargement and fibrosis, atrial inflammatory, and lipid infiltration, as well as changes in atrial electrophysiological properties, ultimately leading to increased rates of spontaneous and induced AF (17). In an ovine model of obesity sustained for 8 months, obesity was associated with infiltration of the left atrial posterior myocardium by epicardial fat and reduced endocardial voltage, representing a potential substrate for AF (18).

In humans, increased BMI has been associated with increased left atrial size (19), which, in turn, is associated with higher AF risk (20). Increased pericardial fat volume has also been described in obese individuals and is related to the presence, severity, and post-ablation recurrence of AF, independent of BMI, suggesting a local pathogenic effect of pericardial fat (21). Obesity has also been associated with increased epicardial fat thickness, which may lead to altered atrial electrophysiology and sympathovagal imbalance of the atria (22-24). Clinically, epicardial fat has been associated with AF (25). Lastly, obesity is a state of chronic, low-grade, systemic inflammation (26). Systemic inflammation has a key role in

**CENTRAL ILLUSTRATION RFM in AF: The Associations Between Cardiometabolic RFs and AF**



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Cardiometabolic risk factors contribute to the development and consequences of atrial fibrillation (AF) and can be modified by weight loss, exercise, and management of comorbid cardiac risk factors. RF = risk factor; RFM = risk factor modification.

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